THE 1936 YEAR CLASS PRIZE IN

SURGERY

"THE IMPACT OF ANTIBIOTICS ON

CURRENT SURGICAL

PRACTICE".

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INTRODUCTION:

Modern surgical practice has been evolving over many centuries, but perhaps the two most outstanding steps, certainly in recent times, have been the introduction of anaesthesia and the antiseptic technique. Both these advances occurred in the Nineteenth Century and completely revolutionised surgical practice. Once the value of antisepsis was appreciated, the emphasis came to be placed on asepsis. The discovery of the role of bacteria in infection led to the chemo-therapeutic advances earlier in the Twentieth Century, and eventually to the introduction of antibiotics. Antibiotics have given medical men powerful weapons to fight the microbes that cause so many diseases. With the aid of antibiotics to prevent and control infection surgeons have been able to undertake operations that would have been inconceivable in earlier years. The sword is two-edged, however, for the use of antibiotics has led to bacterial resistance and the creation of new problems unknown before this era.

After briefly outlining the development of the antibiotic era, consideration will be given to some surgical advances that have been possible as a result of the use of antibiotics, followed by a discussion of conditions in which surgical treatment has been replaced by use of antimicrobial therapy and others where this has not occurred. Some general aspects of the complications arising out of the use

of antibiotics in surgical practice will also be discussed. The field under consideration is so vast that it is possible to discuss only a few aspects.

DEFINITION:

An antibiotic is a substance synthesised by one organism which is toxic to other organisms. An antimicrobial is a chemo-therapeutic substance used to kill or to stop reproduction of micro-organisms. For the purpose of this discussion the term "antibiotic" will be used in the wider sense to include antimicrobials. Antibiotics are either bactericidal or bacteriostatic and may be used topically, orally or parenterally.

HISTORY:

Before the introduction of the antiseptic technique, operations of any kind undertaken in a hospital carried a considerable mortality, largely due to infection. The infections most commonly seen were erysipelas, septicaemia, pyaemia and hospital gangrene. In spite of the introduction of general anesthesia, elective surgery was limited in its scope because of its infective complications. For example, amputations carried a 25% to 65% mortality in civilian hospitals early in the Nineteenth Century, and a 75% to 90% mortality in military hospitals. The result of surgical invasion of joint or body cavities was contemplated with horror.

The story of the development of the antiseptic technique pioneered by Joseph Lister is well known. The discovery

of the role played by micro-organisms by Louis Pasteur and others enabled practitioners of the day to explain how infection came about. The problem was now to find a way of attacking these organisms invisible to the naked eye. Ehrlich wrote in 1906: "In order to use chemotherapy successfully, we must search for substances which have an affinity for the cells of the parasites, and a power of killing them greater than the damage such substances cause to the organism itself, so that the destruction of the parasite will be possible without seriously hurting the organism". Ehrlich introduced arsphenamine to treat syphilis.

In 1935 Domagk discovered the antibacterial action of sulphonamides, and with Fleming's discovery of the action of penicillin in 1928, and its development by Florey and Chain in the nineteen-forties, the antibiotic era was finally ushered in. Since the introduction of penicillin, many different antibiotics have flooded the medical market, and many are now synthesised chemically.

ADVANCES IN SURGICAL TREATMENT.

Surgery of the Gastro-Intestinal Tract:

Major surgery of the gastro-intestinal tract has always been hazardous on account of the risk of infection from the bowel flora. Primary intraperitoneal anastomosis formerly carried a high risk of infective sequelas; peritonitis frequently ensued if there was a leak at the anastomosis site. In 1940 Devine reported a series of resections undertaken for carcinoma of the proximal colon.

Right hemicolectomy carried a mortality rate of 35%, and primary anastomosis in the distal colon, a mortality rate of 30%. A defunctioning colostomy invariably had to be made before resection and anastomosis could be undertaken. This is now not always necessary if the bowel is sterilised of its flora before operation. Sterilisation of the bowel is not possible if there is an obstruction present, and this is an absolute indication for preliminary decompression. Ten years after the figures given above were published, Allan was able to report a mortality of 1.2% from 159 resections for carcinoma of the colon.

The drugs available to sterilise the bowel are the slowly-absorbed sulphonamides, such as phthalyl-sulphathiazole, the streptomycin group of drugs, or the broad-spectrum antibiotics such as tetracycline and chloramphenicol, which have complications of their own, such as moniliasis, staphylo-coccal enteritis and blood dyscrasias.

In 1955 Rowlands published a trial of oral neomycin, a bactericidal drug in vitro, but toxic to the kidneys and the eighth cranial nerve. Little is absorbed from the alimentary tract. A regime of oral neomycin in the pre-operative 24 hours gave complete sterilisation of the bowel in 29% to 45% of patients, varying with the exact dose regimen. No resistant organisms developed. It is now regular practice to give oral neomycin and/or phthalyl-sulphathiazole to patients undergoing major bowel surgery for two to three days before operation. The disadvantages of this practice are shown in the development of staphylo-coccal enteritis and moniliasis, due to the suppression of

the normal bowel commensals which usually keep the pathogens in check. Another danger is the sense of false security which may arise from the belief that the bowel is completely sterilised. The basic rules of colonic surgery should never be relaxed, for as soon as oral feeding is recommenced, the bowel flora returns to normal.

It has also been suggested that the normal bowel flora helps to prevent dissemination of malignant cells in patients with alimentary neoplasia, and such dissemination is more likely in a bowel deprived of its flora in operations involving the handling of a carcinoma.

Port-caval shunts:

Cirrhosis of the liver with associated portal hypertension carries with it a poor prognosis. As a result of the rise in portal venous pressure, the spleen is enlarged and varicosities arise wherever there is a venous anastomosis between the portal and systemic circulations. The most serious of these are oesophageal varices, which develop at the lower end of the oesophagus and at the fundus of the stomach, where the left gastric veins anastomose with the azygos system. Massive haematemesis from bleeding varices carries a very high mortality, owing to the difficulty in controlling the haemorrhage.

Surgical management is possible for a reasonably fit patient with a risk of haemorrhage whereby the portal vein is anastomosed to the inferior vena cava, thus by-passing the cirrhotic liver and relieving the back pressure on the veins. After this procedure these patients are

particularly prone to develop hepatic encephalopathy, which is precipitated by the absorption of nitrogenous substances from the alimentary tract. If there is blood in the bowel from bleeding varices, bacteria act on the haemoglobin and the toxic products are absorbed. To reduce this hazard, patients are given a very low protein diet, supplemented by neomycin to remove the bowel flora.

This principle is illustrated by the following case:

Case 1. Mr. W.J. Aged 54.

This patient had been generally unwell for four months, during which he had lost 1½ stones in weight. There was no history of dyspepsia. Three days before admission he vomited fresh blood five times. He admitted to drinking two to three bottles of whiskey a week for some years.

On examination he was pale and nervous, but not shocked. His pulse was 120 beats per minute, and blood pressure 176/100. His abdomen was very distended and rigid. Free fluid was present in the abdomen. The liver and spleen were both palpable. A few spider naevi were detected, and palmar erythema was marked. The sclerae revealed an icteric tinge.

Emergency gastrografin swallow showed multiple large varices in the lower third of the oesophagus and in the fundus of the stomach.

A diagnosis of hepatic cirrhosis with portal hypertension and oesophageal varices was made. Investigations revealed the following results:

Haemoglobin 9.6 gm.%. E.S.R. 50 mm. W.B.C. 8600.

Prothiombin Ratio: 1:3. Platelets 25,000.

Alkaline Phosphatase: 22 K.A. units.
Bilirubin 3.6 mg.%

Thymol Turbidity: 7 units, S.G.P.T. 52 units/ml.

He had no further haematemesis and he proceeded to operation. The bowel was prepared with neomycin 15 ml. q.d.s. for five days pre-operatively. The portal vein was anastomosed to the inferiod vena cava. Pre-operative portal venous pressure was 300 cm. of water and the post-operative level 225 cm. of water.

Four days after operation he began to get restless and to suffer from paranoid delusions, but these were thought to be delirium tremens rather than encephalopathy. He also developed a respiratory infection which was treated with ampicillin. Neomycin was continued until the tenth post-operative day.

Two days after operation his liver function tests showed the following improvements:

Alkaline Phosphatase: 16 K.A. units.

Bilirubin: 3.9 mg.%. Thymol Turbidity: 4 units.

S.G.P.T.: 56 units/ml.

He continued to make good progress and was transferred to a medical ward seventeen days after operation.

Cholecystitis:

Gall stones in the gall-bladder and common bile duct, with concomitant infection of the biliary tract, is a common condition. Chronic cholecystitis, with acute

exacerbations, is responsible for considerable morbidity, and the ultimate treatment is removal of the diseased gall-bladder and the offending stones. Opinions vary regarding the timing of this procedure, some surgeons preferring to operate in the acute stage; others preferring to allow the infection to settle with medical management, proceeding to surgery later.

The following case illustrates the latter principle, and the use of antibiotics in this condition.

Case 2. Mrs. C.B. Aged 61.

This lady complained on pain of a severe, gnawing character in the right hypochondrium for one month, increasing in severity just before admission. She had anorexia, was nauseated and vomited after taking food of any kind. She complained of pruritus for one week and had noticed that her urine was dark organe and her stools pale. She had lost a stone in weight recently.

On examination she was jaundiced and pyrexial, with a pulse of 88 beats per minute. Her abdomen was tender over the right costal margin, with guarding and a positive Murphy's sign.

Liver function tests showed a raised alkaline phosphatase level of 37 K.A. units, and a serum glutamic pyruvate transaminase level of 144 units/ml, but no other evidence of liver damage. Straight X-Ray of the abdomen did not show any opaque gall-stones. She was treated with pethidine to relieve her pain, and ampicillin 500 mgm. 6-hourly intramuscularly. Within 48 hours her temperature

was normal, her pain settled and there was no jaundice. It was planned to remove her gall-bladder within six weeks of her discharge.

The most common organisms responsible for acute cholecystitis are Escherichia coli and Streptococcus faecalis. An antibiotic to which these are most likely to be sensitive is used, such as ampicillin. The use of antibiotics in this situation to combat the infection means that one need not operate on an acutely inflamed and oedematous structure, but can wait until conditions are more favourable for surgery.

Genito-urinary Surgery:

Carcinoma of the bladder is a disease with a reasonably good prognosis if diagnosed and treated early, but which allows the patient to die a miserable death if left too long. In the latter case, palliative surgery can at least ensure a more comfortable end. An operation that has been performed more frequently in recent years for this condition is total cystectomy and transplantation of the ureters into the lower sigmoid colon, so that urine is passed per rectum. Another indication for this procedure is ectopia vesicae in infants. Two complications that arise are the excessive resorption of chloride from the colon, resulting in a hyper-chloraemic acidosis, and ascending infection of the kidneys from the bowel. These patients can be treated with long-term prophylactic antibiotics active against the bowel flora, or urinary infection can be treated vigorously with antibiotics

once it occurs. There are other methods of urinary diversion, such as ileal conduits, each with their own complications, but the uretero-sigmoidostomy is the only one considered here and is illustrated by the following case.

Case 3. Mr. A.D. Aged 68.

Thirty years previously this patient had a polyp in his bladder treated by fulguration. Three years before admission, after twenty-seven years of freedom from symptoms, he noticed occasional haematuria, occurring at the beginning of micturition or sometimes throughout the stream. Recently it had been getting more frequent with passage of clots. For eighteen months he had had frequency, nocturia, urgency of micturition and difficulty in starting micturition and defaecation.

On examination there was an area dull to percussion below the umbilicus, and on rectal examination a soft mass was felt in the anterior wall of the rectum, above a small prostate.

Cystoscopy revealed a tumour of the bladder. Barium enema showed no obstruction or abnormality of the colon or rectum, indicating that the tumour was not fixed to the bowel. There was no evidence of spread.

The operation of total cystectomy for a large transitional cell carcinoma of the bladder was performed and the ureters transplanted into the lower sigmoid, with a mucosa-to-mucosa anastomosis.

Five days before operation bowel preparation was begun

with sulphathalozole 1 G.b.d. and neomycin 15 mls. t.d.s. Enemata were also administered. Three days post-operatively he developed a pyrexia with oliguria. There was no response to oxytetracycline and ampicillin was given. Six days later he developed diarrhoea. No organisms were cultured from his urine, but staphylococcus aureus was grown from his stools. Methicillin effectively overcame the staphylococcal enteritis. This patient also developed hyperchloraemic acidosis, which was remedied by taking sodium bicarbonate and potassium citrate. He was not discharged on any antibiotic as his urine had not shown any sign of infection.

In one study of this procedure published by Jacobs and Stirling in 1952, the overall mortality was 21%. The common complications were leakage, urinary tract infection and stenosis. The presence of a leak causes an inflammatory reaction with resulting stenosis and ascending urinary infection. It was found that patients who had electrolyte disturbances generally had pyelonephritis also, and if there was no eletrolyte imbalance, there was generally no renal infection. This has been attributed to the fact that healthy kidneys will excrete the excess chloride absorbed in the urine, whereas pyelonephritic kidneys will not do this efficiently.

Two examples of major surgery have been quoted - namely, porta-caval shunt and ureteric transplant - in which antibiotics play an important part and which can now be offered to patients with incurable diseases with a moderate

prospect of success. Another field in which great advances have been made in recent years is that of organ transplantation, in particular renal transplantation.

Renal Transplantation:

The technical problems of the actual transplantation have now largely been overcome. The most important problem at the moment is that of rejection of the transplant: the immunological response of the nost to a foreign organ. This natural response can be overcome temporarily by irradiation and immuno suppressive drugs, such as azothioprine (Imuran) and cortico-steriods. The ability of the host to combat foreign tissues by the production of antibodies is thereby suppressed. The patient is, therefore, particularly susceptible to all forms of infection, especially in the immediate post-operative period when high doses of immuno-suppressive drugs are given. Prophylaxis is of the utmost importance in these patients. As will be seen later in this discussion, prophylactic use of antibiotics is not an effective means of preventing infection, and more efficient measures must be taken. The sources of infection are either exogenous or endogenous, and the former is the only one against which one can take preventive measures effectively. These are chiefly of a physical nature: the patient is isolated in a room, itself in an isolated sterile area and everything coming into the area is sterilised and everyone entering takes a shower and dons sterile clothing, caps and masks. All used and soiled objects leave the room by a different route so that there is one-way traffic

at all times. These measures can reduce the rate of infection in patients with renal transplants to a very low level. Of those receiving transplants in Edinburgh, the few that have succumbed to infection have derived it from endogenous rather than exogenous sources. The use of antibiotics is reserved for cases where infection is proved and adequate doses of a drug to which the organism is susceptible are used.

THE CHANGING PATTERN OF SURGICAL CONDITIONS.

Antibiotics have not only allowed newer and more major operations to be performed, but they have themselves been used in the treatment of conditions which formerly could only have been treated surgically, but which are now seldom seen in the surgical wards of Britain to-day.

One outstanding example is tuberculosis. Pneumonectomy and lobectomy were not infrequently performed to remove tuberculous lung tissue which could never function again, and could serve only to damage the patient. Tuberculous empyema was treated by thoracotomy and decortication of the lung. The lung was not uncommonly collapsed by artificial pneumo-thorax to "rest" the diseased tissue. Since the introduction of streptomycin twenty years ago, followed by the other anti-tuberculous drugs, not only have the indications for surgery in this condition become considerably less, but also the incidence of tuberculosis in this country declined remarkably.

Renal tuberculosis at one time invariably called for nephrectomy. In 1963 Hanley estimated that chemotherapy for renal tuberculosis resulted in 60% sterile urine after two months and 80% after three months. Between 1951 and 1961 over 440 patients in his study received triple therapy for six months in a special unit, together with any necessary conservative surgery, and para-amino salicylic acid and isoniazid for a further eighteen months at home. Only four out of the 440 completing the full course relapsed. The principle of treatment here is that the tubercle bacillus is destroyed if the correct drug comes into contact with it for a long enough period of time. If chemotherapy fails, either the wrong drug is being used, the patient is not taking the drugs, or the healing fibrosis creates avascular caseous areas inaccessible to drugs. In the latter case, surgery is required to remove this avascular tissue, and, if necessary, to relieve obstruction. Procedures such as cavernotomy, re-implantation of the lower end of the ureter, and plastic procedures at the pelvi-ureteric junction are the ones more frequently used to-day. The chief indication for total nephrectomy is pelvi-ureteric obstruction.

A similar story can be related for <u>osteomyelitis</u>, for antibiotics have noticeably decreased the morbidity and mortality from this disease, both by controlling the osteomyelitis itself and other infections which lead to osteomyelitis. Early diagnosis is the essential point

in this condition, for antibiotics are ineffective once there is necrotic tissue within the bone, until it is removed.

There has also been a change in policy towards respiratory infections. Common complications of pneumonia before the introduction of antibiotics were empyema, lung abcess and bronchiectasis, all of which required surgical management. Early treatment of pneumonia with appropriate antibiotics prevents the occurrance of these late sequelae. Lung abcess may develop, particularly after staphylococcal pneumonia, and as this is becoming increasingly difficult to treat with the emergence of resistant organisms, surgical wards may see more of this condition. Antibiotics are not effective if the organisms are allowed to remain in an environment conducive to their continued multiplication, as in stagnant secretions or necrotic tissue. A most important part of the management of respiratory infections is the removal of secretions by coughing, postural drainage or aspiration by bronchoscopy or tracheostomy if necessary.

Antibiotics are obviously powerful weapons to use against bacteria, but once the infection is localised and an abscess formed, with pus in the cavity, and a capsule of fibrous and granulating tissue around it, there is only one treatment - aptly summarised in the aphorism "Where there is pus, let it out". It has been said in recent years that there has been a tendency to forget the proper place which surgery should take in the treatment of infection, because so much attention has been focussed on the development of antibiotics.

An example of this principle is seen in breast abscesses. If antibiotics are given within the first 24 hours of the infection, when the process is still a cellulitis, the infection may be aborted. After that time an abscess will invariably form and the most effective form of treatment is to allow the process to continue until there is an efficient protecting capsule and fluctuation can be elicited. At this stage the abscess should be incised and adequately drained. Continued treatment with antibiotics without surgery results in an abscess cavity filled with sterile pus, with no possibility of resolution. This has been aptly termed an antibioma.

Another example is that of hand infection. The serious types, such as acute infective teno-synovitis, and deep infections are not so commonly seen. If the patient is seen when the infective process is still a cellulitis, appropriate antibiotic therapy may abort the infection, together with immobilisation of the hand and elevation. If there is throbbing pain, acute tenderness, loss of function and constitutional disturbance, indicating abscess formation, surgical drainage is imperative. A few hours' treatment with antibiotics before operation will combat the systemic upset and the cellulitis surrounding the abscess. The staphylococcus is the most common organism involved in hand infections, and the streptococcus but rarely. The streptococcus is the only organism that will cause an ascending lymphangitis, and surgery should never be required, as penicillin is an effective antibiotic against this organism. One cannot wait in hand infections

for bacteriological resports, so antibiotic therapy must be empirical initially. The choice varies with locality. In the Edinburgh area erythromycin has been found to combat the staphylococcus successfully. This method of treatment is suitable particularly for paronychia (which is frequently due to yeasts), pulp space and subcutaneous infections.

POST-OPERATIVE COMPLICATIONS.

Wound Infection:

Sepsis in wounds is a perennial problem, and is particularly common after surgery on the bowel. Incidence varies greatly, Rousselot and Slattery recording 15%, but others giving figures higher than that. In a recent article Nash and Hugh assume that most wound infections occurring after colonic surgery are initiated at operation and the source of the organisms is the large bowel. Coliforms, Clostridia, Bacterioides and Staphylococcus aureus are the organisms usually responsible.

In 1960 a survey in twenty-one hospitals in England and Wales revealed a 9.7% incidence of post-operative wound sepsis, the rate varying from 4.7% to 21.8% in general surgical wards. The highest rates for "clean" operations were 21% for cholecystectomy and 15% for breast operations. The lowest rate was 2% for orthopaedic operations. Increased rates of sepsis were found with increasing age, length of pre-operative stay, length of incision, duration of operation and the presence of drainage tubes. Nasal carriers of staphylococci had a

higher sepsis rate than non-carriers. The organisms most frequently responsible were staphylococci and coliforms. Wound infection meant a stay of 7.3 days longer in hospital on an average.

In the Edinburgh Royal Infirmary a 9.8% incidence of serious infection and a 16.3% incidence of trivial infection were found in 673 clean wounds in four surgical charges in 1956. The highest rate of serious infection was found in the general surgical wards.

Wounds may become infected either by deposition of organisms at operation, by airborne spread from carriers of organisms or other infected patients, by contaminated inanimate objects or by the patient himself, particularly if he harbours organisms somewhere else in his body. Much has been written about the control of contamination, particularly by staphylococci, with emphasis on eradication of carrier states, strict aseptic techniques, efficient cleaning and ventilation systems and so on. What part do antibiotics play in this field?

The staphylococcus is notorious for its ability to acquire resistance to a large number of antibiotics, the first being penicillin. Pseudomonas pyocyanea, an organism occurring with increasing frequency on surgical wards, is inherently resistant to most antibiotics. Finland, in 1960, studied the bacterial situation in general. The figures he quoted all came from the Boston City Hospital.

Table 1.

Organism responsible	Proportion of all bacteraemic patients		Proportion of deaths in bacteraemic patients	
	1935	1957	1935	1957
Pneumococcus	34.5%	14.1%	46.7%	10.4%
B. haemolytic streptococcus	18.3%	3.6%	23.4%	1.4%
Staphylococcus aureus	22.4%	38.6%	18.6%	40.1%
Normal bowel inhabitants	11.7%	34.5%	9.0%	47.7%
Others	21.0%	16.8%	22.0%	17.1%

From this table it can be seen that bacteraemis resulting from staphylococcal and coliform infections increased over the period considered, whereas the pneumococcus and streptococcus were becoming less common. The greatest increase in staphylococcal bacteraemia has been since 1951, when chloramphenicol and the tetracyclines became available. Bacteraemia due to normal bowel commensals has also increased. It is possible that organisms which were of virulent nature and the cause of serious illness before the introduction of antibiotics were very susceptible to these agents, as shown by the statistics for pneumococcal and streptococcal infections. Other organisms not commonly seen before this era are now able to manifect themselves and they are more difficult to eradicate. The surgeon's problem to-day, therefore, is the increasing incidence of wound infection due to organisms that are not susceptible to antibiotics, either due to intrinsic resistance or to mutation as a

result of excessive use of antibiotics. As more patients are treated with antibiotics, there is a greater risk of transmitting resistant strains to other patients.

Prophylaxis.

The place of prophylaxis of infection may well be considered here. In theory this is ideal - to prevent infection, with all its attendant complications, occurring in patients at risk.

The prevention of spread of staphylococci by staff and patients can in part be achieved by applying topical antibiotics to the anterior nares and other carrier sites. Skin disinfection can be achieved with hexachlorophene soaps and soframycin cream. Spraying of surgical wounds at the end of operation with Polybactrin may also decrease the incidence of wound infection. Recently a trial was performed to assess the effects of topical application of ampicillin in preventing wound sepsis after colonic surgery. It was found that 41% of the untreated group became infected and only 3% of the treated group. The authors recommend that because of its low toxicity, this broad-spectrum drug can be used in fairly large quantities in this way, thereby inhibiting strains of E. coli and other organisms resistant in vitro to the lower concentrations achieved with systemic therapy. There is, unfortunately, a high incidence of skin hypersensitivity reactions when the penicillin group of drugs are used topically.

Prophylactic antibiotics used systemically after operation have been shown to be ineffective and are not

recommended because of the danger of super infection and emergence of resistant organisms. In relation to the bowel, it is possible that the normal mixed microbial flora inhibit other more pathogenic organisms. For example, E. coli found in the bowel suppresses the growth of Candida albicans in vitro, but if tetracycline is added to the culture medium the E. coli are suppressed and Candida albicans flourishes.

In a few instances systemic use of antibiotics prophylactically is of value. One clear indication for their use is in the prevention of subacute bacterial endocarditis in patients with valvular lesions of the heart who are undergoing dental surgery. Penicillin is effective in these people. In twenty-three trials where antibiotics were used to prevent post-operative wound and chest infections, only six were able to show a decreased incidence of sepsis. A general rule is that antibiotics should be used to combat proven infection, and then they should be specific and given in adequate dosage for sufficient length of time.

The following case illustrates some points already discussed regarding antibiotics therapy.

Case 4. Mr. T.B. Aged 54.

This patient was admitted to hospital complaining of an intermittent, stabbing, epigastric pain lasting for a few minutes at a time and aggravated by coughing or vomiting. He was anorexic and constipated, with one bowel motion in six days. He had not noticed melaena or steatorrhoea. He admitted to drinking 4 to 5 pints of beer a day.

On examination he was unkempt and cachectic, conscious but drowsy. His pulse was regular, at 108 beats per

minute. Blood pressure was 120/50. There were no signs of cardiac failure. His tongue was dry and furred. Abdominal examination revealed limited movement on respiration, marked tenderness to the left of the umbilious and guarding in the umbilical area. Bowel sounds were hypoactive.

Straight X-Ray of the abdomen showed diffuse calcification of the pancreas, and the serum amylase was 357 Smorgyii units. In addition, serum calcium was 8.4 mg/100 ml, bloo urea 70 mg/100 ml, serum potassium 2.6 m Eq/l and serum bicarbonate 37 m Eq/l. Blood sugar was normal. A diagnosis of acute pancreatitis was made and he was treated conservatively in the conventional way with Omnopom, Propanthylene, Trasylol and Oxytetracycline 200 mg. 6 hourly intramuscularly.

Four days after admission his abdomen was still tender, but he continued to progress slowly. Thirteen days after admission he developed severe diarrhoea, with green watery stools, which grew staphylococcus aureus on culture. In a few hours he was in circulatory collapse and very dehydrated and required large quantities of intravenous fluid. He was given neomycin and methicillin, which was later changed to ampicillin. Four days later he developed bronchopneumonia and renal failure with oliguria, a combination which proved fatal.

At autopsy, a necrosed haemorrhagic pancreas was found, confirming the original diagnosis.

It is now recognised that surgery is generally not of value in acute pancreatitis and the aims of conservative treatment are to put the bowel and pancreas at rest by

intravenous feeding and decreasing secretions and motility with Propanthylene. The development of peritonitis is a real danger, and a tetracycline is given prophylactically to avoid this complication. In this patient's case peritonitis was avoided, but an acute staphylococcal enteritis developed instead, leading to circulatory collapse. This illustrates the hazard of using a broad-spectrum antibiotic prophylactically.

Burns.

The problem of infection is constantly present in the management of burns, whether treated by the open or closed method. Sloughing necrotic tissue is an ideal culture medium for bacteria, and the destruction of the cutaneous barriers increases the risk of colonisation by pathogenic organisms. It is important to prevent infection in these severely ill patients who are at risk. Control of bacterial invasion gives better clinical results. In 1960 Cason and Lowbury from the Birmingham Accident Hospital studied prophylactic antibiotics in cases of burns. They used a cream composed of neomycin, chlor-hexidine and polymyxin (N.C.P.) with tulle gras as a control dressing. Infection with staphylococci and streptococci was less common in burns treated with NCP cream and the healing time of split skin grafts in cases of full thickness burns was shortened by an average of eleven days. Infection with Pseudomonas sp. was not common if either NCP cream or tulle gras was used. Gram negative organisms were better controlled by drying the

area. It was found that staphylococcal and Gram negative infection was more frequent if antibiotics were given systemically. If chloramphenicol or tetracycline was used topically, the numbers of resistant staphylococci increased. The authors of this study concluded that the most important bacteria in burns did not become resistant to NCP cream. It is general policy, however, that the treatment of established infections decreases the reservoir of pathogens and, therefore, of self- and cross-infection.

Other trials have demonstrated the effectiveness of neomycin and chlorhexidine tulle in dressing burns, as opposed to penicillin cream, resulting in less infection with staphylococci and the Gram negative organisms. In burns treated by exposure it has been shown that the prophylactic use of polymyxin, neomycin and bacitracin (Polybactrin) sprayed from a pressure pack resulted in less infection than penicillin lactose powder or not antibiotic. However, the results of skin grafting in these patients was less good than those treated with penicillin cream.

Controversy will continue on the subject of prophylactic antibiotics, particularly in relation to surgical wounds and burns. The excessive use of antibiotics in the early days of their availability has partly resulted in the problem of infection with organisms which are becoming increasingly difficult to eradicate. To try to lessen the occurrence of resistant organisms, antibiotics should, in general, be used to combat proven infection. The ability to control infection in wounds and burns has improved the outlook markedly for

these patients, and it is vital that the agents which are used should remain effective.

The problem of post-operative wounds and burns, together with the place of antibiotics in this problem, has been dealt with at length, because it is of great importance wherever surgery is practised. Some other post-operative complications will now be considered briefly.

Respiratory Infection.

Middle-aged men who smoke have chronic bromchitis and emphysema, and who undergo upper abdominal or thoracic surgery or repair of herniae, are ideal candidates for post-operative chest infection. The pain of the wound, drowsiness after the anaesthetic and their posture in bed all make them disinclined to cough. Secretions accumulate and block the bronchioles or bronchi and cause collapse of lobules or even a lobe of the lung. Infection rapidly follows obstruction and collapse. Vigorous physiotherapy and adequate analgesia may prevent this sequence of events, and are essential once it has occurred, together with an antibiotic in adequate dose, acting specifically against any organism found in the sputum. Until an organism is isolated, it is customary to give a broad-spectrum antibiotic, such as ampicillin, to cover a wide range of organisms. Antibiotics are ineffective if secretions remain accumulated to continue the obstruction. With the availability of antibiotics and better understanding of the importance of removing secretions, the mortality from post-operative respiratory complications, and morbidity from the develop-

ment of chronic suppuration, such as bronchiectasis and lung abscess, has undoubtedly fallen.

Urinary Tract Infection.

Infection of the urinary tract is particularly common after prostatectomy or bladder surgery. It is also a common complication of catheterisation, and emphasis on this fact has led to the advocation of avoidance of catheterisation unless absolutely essential, because of the appreciable risk of introducing pathogenic organisms into the urinary tract. Another complication of prostatectomy is transference of infection along the vasdeferens to the epididymis and testis. To prevent this particular complication, some surgeons ligate the vas at operation.

It has been found that urinary infection after prostatectomy can be reduced by the use of a closed apparatus for aseptic drainage and irrigation of the bladder. Disinfecting non-boilable cystoscopes with chlorhexidine and mercuric cyanide also reduces the risk of infection. Preventive measures such as these reduce the load of infection due to antibiotic-resistant organisms, as is seen by the decreased incidence from 74% to 23% in the British Royal Infirmary.

Chemotherapy is no substitute for methods aimed at preventing infection. Once infection has established itself in the urinary tract it can be difficult to eradicate. The antibiotic must reach satisfactory concentrations in the renal parenchyma and the urine, and failure to achieve this results in the emergence of resistant organisms. The problem is complicated by the fact that about one-third of

the patients who undergo surgery for the prostate or bladder are already infected. Stagnant urine, which of itself cannot lead to infection, readily does so when contaminated by catheter or cystoscope.

The problem of urinary infection is also of concern in parturition. Brumfitt estimated that the incidence of urinary tract infection in normal labour without catheterisation was 4.7%;in normal labour with catheterisation 9.1% and in complicated labour with catheterisation 22.8%, a striking increase. The suscepitibility of the pregnant woman to urinary tract infection is an additional hazard.

Urinary tract infections are, therefore, not uncommon in surgical practice, and prevention is much more satisfactory than treatment with antibiotics.

Peritonitis.

One of the greatest hazards of intra-abdominal surgery in days before the introduction of antibiotics was peritonitis. The mortality from this serious complication has considerably decreased with the better understanding of fluid and electrolyte balance, and the use of antibiotics. Peritonitis may, of course, arise secondary to some other condition, without surgery. An example is the peritonitis that occurs after a perforated peptic ulcer, and the treatment is primarily surgical. The organisms responsible are usually found in the bowel - E. coli, anaerobic streptococci, clostridia and bacterioides. In one investigation, of 111 cases with pus in the abdomen, Bacterioides were found in 67, E. coli in 66, anaerobic and aerobic streptococci in 43 and 40

respectively. The Bacterioides were all sensitive to tetracycline and chloramphenicol, and most to sulphonamides and erythromycin. Some maintain that tetracycline is superiod to penicillin and streptomycin in the management of peritonitis.

The mortality rate from peritonitis decreased notably in the decade preceding 1949, chiefly on account of earlier diagnosis, improved anaesthesia, better understanding of fluid and electrolytes in stress and disease, and hemo-therapy. The trend has not continued, as seen in the 3,887 deaths from peritonitis recorded in England and Wales in 1949 compared with 4,311 in 1958. In the last ten years at the Hammersmith Hospital it is recorded that the mortality rate from tyis condition has doubled, due to several factors including the increase in antibiotic-resistant organisms. Early effective treatment of peritonitis is, therefore, imperative. An early operation while the peritonitis is still aseptic (the first 6 to 8 hours) can remove or shut off the source of organisms, as in repair of a perforated peptic ulcer. Aspiration of the infected exudate and drainage of the site of the lesion will also lessen the risk of progression of the condition. The use of two broad-spectrum antibiotics such as tetra-cycline and erythromycin will increase the chance of effectively combating the causative organism.

The need for antibiotics may occur as a result of other forms of treatment. One example that is becoming increasingly common is seen with the use of cortico-steroids for a large number of conditions. One of the many side

effects of steroid therapy is an increased susceptibility to infection, which may present in a bizarre way, due to the diminished inflammatory response. Once infection has occurred, vigorous antibiotic therapy is required. Most of these cases are seen in medical wards, but two that may be seen in the surgical field may be mentioned.

Bilateral adrenalectomy is occasionally performed for reasons such as hyperplastic changes in the adrenals, or to relieve the pain of metastatic breast carcinoma. In these patients inadequate replacement therapy may lead to an increased susceptibility to infection, and once infection is established, even with adequate therapy for normal purposes, an Addisonian crisis may be precipitated. Corticosteroids to meet the addition stress, and antibiotics to combat the infection, are required.

Baker et al. from the Royal Post-graduate School of Medicine reported recently the cases of two patients who were receiving steroid therapy, and who had a neutropaenia. These patients developed osteomyelitis which required surgical drainage. The authors point out that infections occurring with steroid therapy usually progress rapidly and silently, and, in skeletal infections, lead to extensive destruction and necrosis. Such infections do occur and may require surgical treatment.

Conclusion.

Only a small part of the field under discussion can be considered in one essay. Infections due to viruses and parasites are also seen in surgical practice, but antibiotics

are not usually of value in dealing with them. The question of infection of prosthesis, such as artificial heart valves, has not been considered.

However, it is hoped that from this discussion it can be seen that the use of antibiotics has allowed some surgical advances to be made. The pattern of conditions treated surgically has changed with the use of antibiotics, but some instances have been considered where surgical treatment is essential. The use of antibiotics has created its own problems of emergence of resistant organisms. Antibiotics can never replace effective preventive measures against infection, and the chief indication for their use is in established and proven infection where, if used intelligently, they may prove to be valuable weapons.

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